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PUBLIC HEALTH REPORTS.

UNITED STATES.

[Reports to the Surgeon-General, Public Health and Marine-Hospital Service.]

NOTES ON RAT LEPROSY AND ON THE FATE OF HUMAN AND RAT LEPRA BACILLI IN FLIES.

[By Acting Assist. Surg. Wm. B. Wherry, Oakland, Cal.]

The idea that parasitic insects might play some rôle in the transmission of leprosy seems to have existed for some time. More or less presumptive evidence in the case has accumulated and this has been well reviewed by Nuttall,^a who says: "It appears that Linnæus and Rolander considered that *Chlorops (Musca) lepræ* was able to cause leprosy by its bite. Blanchard^b and Corredor^c tell of flies in connection with leprosy, citing the case of an Indian who had lived some time with lepers and acquired leprosy, as he himself claimed, through the agency of flies. The insects gathered frequently in great numbers on the ulcers of his leprosy comrades and some of these insects bit him. The first leprosy ulcers appeared on the places where the insects had inflicted wounds. Joly^d says his teacher Sabrazes has long held the view that leprosy might be produced by a large number of small inoculations, such as insects, especially parasites, may inflict. This, he considers, seems probable because of the large numbers of lepra bacilli which are present in the skin and ulcers in cases of cutaneous leprosy. Insects could scarcely avoid taking up the bacilli in sucking the blood or the exudations from the ulcers of leprosy subjects and might transfer and inoculate the germs into healthy individuals. He seems inclined to attribute a part of the leprosy which prevails, especially among the poor and unclean classes, to the agency of cutaneous parasites which are often found among them. An observation of Boeck on the presence of *Sarcoptes scabiei* in a case of cutaneous leprosy led Joly to conclude that these parasites might at times serve as carriers of the infection. It appears that these parasites are very frequently found in Norway in places where much leprosy exists; they, as also *Pediculi*, are usually present among the poorer classes in Algeria, which furnish the greater number of lepers. In Sudan, the *Sarcoptes* occur on almost all the dogs and often attack the natives, among whom there are numerous

^a Nuttall, G. H. F., The Rôle of Insects, Arachnids, and Myriapods, as Carriers in the Spread of Bacterial and Parasitic Diseases of Men and Animals, Johns Hopkins Hosp. Reports, 1907, 8, pp. 1-154.

^b Blanchard, Zool. Med. II, p. 497.

^c Corredor, Revista méd. de Bogotá, reviewed by Polakowsky in Deutsche med. Wochschr., Sept. 30, 1897, p. 646.

^d Joly, Thèse, Bordeaux, 1898, p. 67.

lepers. It seems to me that the possibility of this mode of transfer can not be denied, and it is also conceivable that the pathological changes produced in the skin by the parasites may even favor the multiplication of the lepra bacilli. Finally Sommer,^a of Buenos Ayres, expresses the belief that mosquitoes probably act as active agents in the spread of leprosy in warm countries, but this is very unlikely."

Again, according to Baker^b "the interest in this subject is further accentuated by the statement that Doctor Carrasquillo, of Bogota, has found the bacillus of Hansen in the intestinal contents of fleas. It is thus open to question if the fleas are not the agents for the communication of leprosy."

Further, Dr. W. J. Goodhue and his assistant, Father Joseph, working at the leper settlement at Molokai, Honolulu, made many dissections and stained preparations from mosquitoes and finally found lepra bacilli in the intestinal contents of a female *Culex pungens*. Later they found similar organisms in the common bedbug (*Cimex lectularius*).^c

It is related that the British leprosy commission investigated the possible rôle played by insects with entirely negative results. I have been unable to consult their reports.

My interest was aroused in the possibility of blood-sucking insects playing some rôle in the transmission of leprosy during my studies upon the leprosy of rats. That this disease occurs among Norway rats (*M. norvegicus*) on the Pacific Coast has already been pointed out by me.^d

While detailed to plague work in Oakland, Cal., careful search was made for leprosy in rats in order to gain some idea as to its prevalence. During the four months between April 15 and July 15, 1908, 9,361 rats were dissected. Of these 20 were infected with leprosy. Nine were females and 6 males, and in 5 the sex was not recorded. The experience gained in recognizing the anatomical features of the disease resulted in the recognition of some cases of very recent infection. It seems probable, therefore, that few, if any, leper rats were overlooked in this series. Most of these rats, however, were very large, old rats, which showed such marked alopecia and superficial ulceration, with occasional atrophy of the tail or toes of the feet, as at once to excite suspicion. To illustrate the sickly and defenseless condition of rats in an advanced stage of this disease, I might relate that one leper rat was found staggering about in an apparently half blind and defenseless condition on one of the public streets of Berkeley in broad daylight. Judging from the results of experimental inoculation, the two early cases of naturally acquired leprosy examined by me must have been of six to eight months' duration. The only lesions present were in the axillary glands in one case and in the inguinal in the other and the subcutis immediately adjacent to these regions. The submaxillary and cervical glands have never been found infected even in the most advanced cases.

^aSommer, Leprosy in the Argentine Republic, *Semana Médica*, June 23, 1898, reviewed in *Jour. Amer. Med. Assoc.* Sept. 10, 1898, p. 618.

^bCarl F. Baker, The Classification of the American Siphonaptera, *Proceedings of the U. S. National Museum*, 1905, 29, 122.

^cReferred to by Dr. E. S. Goodhue—Mosquitoes and Their Relation to Leprosy in Hawaii, *American Medicine*, new series, 1907, Vol. II, No. 10, pp. 593-598.

^d*Jour. American Med. Assoc.*, 1908, 50, 1903.

Various possible modes by which the disease may be transmitted from rat to rat suggest themselves. Myriads of lepra bacilli lie just beneath the Malpighian layer of the epidermis in advanced cases. These might be transferred by blood-sucking parasites, *Siphonaptera*, *Pediculidae*, or *Tabanidae*, which so frequently attack sickly animals in unusual numbers. Then, as in human leprosy, the bacilli sometimes escape in considerable numbers with the nasal secretion. In my series, out of six examinations of the mucosa of the posterior nares, lepra bacilli were found three times; twice they were numerous and once few in number.

Again, a leper rat's teeth might become instruments of inoculation, either through contamination from the posterior nares or during the rat's process of ridding itself of insect parasites, or of licking its ulcers. Further, infection may occur through the gastro-intestinal tract either through feeding upon the bodies of dead leper rats or through foodstuffs contaminated by leper rats. McCoy^a reports finding lepra bacilli in the bladder of one rat. Examination of the contents and mucosa of the bladder in four advanced cases, made by myself, were negative.

The character of the lesions present early in naturally acquired cases of this disease, seems to point to inoculation through the skin. Ecto parasites were very scarce upon the rats as they were all brought in dead. One *Ceratophyllus fasciatus*, one *Ctenopsyllus musculi*, one rat louse (*Hænatopinus acanthopus*), and one cone-nosed Arachnidian were carefully ground up on slides and stained for lepra bacilli without results. Only one nematode has been encountered in sites where the lepra bacilli occur and this is a filaria-like worm, about 20 mm. long, sometimes found in the posterior nares of *M. norvegicus*.

The presence of enormous numbers of lepra bacilli in the excretions of the cutaneous ulcers suggested the possibility of their being taken up by flies. The ability of lepra bacilli to multiply and persist within a fly after the manner of tubercle bacilli^b could only be affirmed or doubted after actual observations on this point.

EXPERIMENTS WITH FLIES.

1. *The fate of lepra bacilli in flies fed on the carcass of a leper rat.*—The carcass of leper rat No. 4 was found on May 20, 1908, in a cellar beneath a grocery store. It was apparently 2 or 3 days old and badly fly-blown, a large female *M. norvegicus*, showing marked alopecia, multiple ulcerations of the skin which was thickened especially about the regions of the axillæ, and hyperplasia of the cutaneous, axillary, and inguinal glands. Smears showed enormous numbers of lepra bacilli in the subcutis, cutaneous ulcers, and axillary and inguinal glands. After dissection the carcass was placed in a large glass jar, and exposed to flies. When a number of flies had collected within the jar it was quickly screened. The flies were chiefly green bottle flies (*Lucilia Caesar*), blow flies (*Calliphora vomitoria*), and a few house flies (*Musca domestica*). After feeding upon the rat's carcass, the flies deposited specks upon the sides of the glass jar. Examination of the

^a McCoy, Public Health Reports (United States), 1908, Vol. XXIII, No. 28, July 10.

^b See Flies and Tuberculosis, Publications of the Mass. Gen. Hosp. 1906, 1, 118, for the work of F. T. Lord and his predecessors.

specks deposited during the first twenty-four hours after feeding showed that the flies took up enormous numbers of lepra bacilli and deposited them with their feces. These flies were then removed to a clean jar and fed upon the liver of a normal rat. Examination of the specks deposited during the second twenty-four hours showed that the lepra bacilli were almost completely voided during the first portion of this period, *i. e.*, the old dry specks were the only ones which contained acid-proof bacilli, and even these contained them in greatly diminished numbers. The fresh moist specks (deposited forty to forty-eight hours after the ingestion of lepra bacilli) were almost invariably clear, though occasionally 2 or 3 acid-proof bacilli resembling lepra bacilli could be found.

2. *The fate of lepra bacilli in the larvæ, pupæ, and imagoes of flies hatched in the carcass of a leper rat.*—Larvæ which had hatched out in the rat were washed by shaking in repeated changes of salt solution, or bouillon, and dissected. The vast majority of those examined contained enormous numbers of lepra bacilli. To determine whether the bacilli would persist in the insects through the stage of pupation and appear in the imagoes, two series of experiments were performed.

Series I. To determine whether the bacilli would persist when the larvæ were fed upon uninfected meat.—One hundred and fourteen large and small larvæ were removed from the carcass of the leper rat, placed in a clean jar and from time to time fed on the livers of normal guinea pigs and rats. Examinations of some of these larvæ were made at intervals after their removal, *e. g.*, two larvæ examined five days and one six days after removal showed no lepra bacilli. The larvæ and pupæ were kept at room temperature. The pupæ were kept separated in flasks and when the flies hatched out they were fed on uninfected meat and their specks examined for lepra bacilli. The following table gives some of the details of these observations:

Number of pupa.	Number of days after rat was fly-blown till pupa appeared.	Number of days after pupation until fly hatched out.	Kind of fly.	Age of fly when specks were examined, in days.	Results.
1	10	23	<i>C. vomitoria</i> ..	1	0
2	10	26do	5	Fly died.
3	10	11do	1	0 (died).
4	12	26do	4	0 (died on 5th day).
5	13	25do	1	4 lepra bacilli found in speck.
				(a)	Show quite a number of lepra bacilli in clumps. The bacilli appear quite segmented. (This fly was fed on meat, and its specks examined a few hours later showed no lepra bacilli.)
6-15	15	13-14do	1	0

^aSpecks deposited immediately after hatching.

Series II. The fate of lepra bacilli in the larvæ fed almost continuously on the carcass of a leper rat and in the pupæ and imagoes developing therefrom.—The rat carcass, alive with maggots, was kept at

outdoor temperature in a screened jar. A drop in the temperature delayed pupation. Three larvæ were examined twelve days from the beginning of the experiment, and all contained numerous lepra bacilli. Eight pupæ (4 partially dried and 4 normal) were examined thirty-one days from the beginning of the experiment, and all contained numerous lepra bacilli; in two they were very numerous.

Twenty-two blowflies (*C. vomitoria*) hatched out on the forty-third day from the beginning of the experiment. The specks of 15 of these, deposited during the first twenty-four hours after hatching, contained no lepra bacilli. The specks of 6 others, deposited during the first three days after hatching, contained no lepra bacilli. One fly died without depositing any specks, and this one, with a number of others, was dissected with negative results.

Thousands of pupæ in the jar remained unhatched and were under observation for a month and a half. Some of these were dissected and found to contain numerous lepra bacilli on the forty-third day from the beginning of the experiment. So it would seem as if these heavily infested pupæ were incapable of undergoing further development.

3. *The fate of lepra bacilli taken up by flies from the leprous ulcers on a human case.*—While visiting the lepers at the Alameda County Infirmary, on June 9, 1908, I caught two house flies (*Musca domestica*) upon the face of an advanced case of nodular leprosy with ulceration of the nodules about the nose. The specks deposited in the vial within an hour after the flies were caught were examined and in one speck two lepra-like bacilli were found. During the first twenty-four hours after their capture the flies deposited numerous specks upon the sides of the vial. Five out of 6 of the specks examined showed considerable numbers of lepra-like bacilli, occurring singly and in clumps of 20 to 50 rods. The flies were transferred^a to a clean flask and within an hour and a half there were three specks in the flask. These were deposited on the morning of June 11, or one and one-half days from the time the flies were captured. Two of these specks were examined and both contained many lepra-like bacilli. The flies were then separated and it was found that only one of them, No. 2, was infested with acid-proof bacilli. The specks deposited by this fly on June 12, three days after its capture, also contained numerous lepra-like bacilli. Six specks deposited by this same fly between the third and sixth day of its captivity were carefully examined and only one lepra-like bacillus was found. The fly died on the sixth day.

Determination of the number of lepra-like bacilli in a single fly-speck.—One of the specks deposited by fly No. 2 on the third day of its captivity was carefully removed and emulsified on a slide with a small drop of a suspension of typhoid bacilli. This was then spread over a square area with the point of a needle, stained by the tubercle method with a contrast of Löffler's methylene blue, and the number of acid-proof bacilli were counted with the aid of a Zeiss mechanical stage. Eleven hundred and fifteen lepra-like bacilli were counted, but this does not account for the real total, owing to the fact that the bacilli often occurred in clumps and it was impossible to count all of them.

^a The transfer of flies from flask to flask is a matter of clock-like precision and simplicity if it be remembered that flies are strongly heliotropic.

The determination of the probable nature of these acid-proof bacilli.—The question of course is, May not these have been simply tubercle bacilli, or even, perhaps, some other acid-proof bacillus than the lepra bacillus? No attempt was made to cultivate these bacilli. However, numerous specks deposited during the first and second days of the flies' captivity were emulsified in salt solution. This suspension, which showed quite a large number of lepra-like bacilli, was injected on June 11 into the abdominal subcutaneous tissue of a guinea pig weighing 540 gms. July 11 the guinea pig weighed 570 gms. and showed no local reaction nor enlargement of the glands. August 8 it weighed 480 gms. and showed no signs of infection. August 22 it weighed 502 gms. September 14 it weighed 540 gms. September 10 it was given $\frac{3}{100}$ mg. of Koch's old tuberculin subcutaneously without a reaction. It was chloroformed and found perfectly normal.

THE RELATION OF RAT TO HUMAN LEPROSY.

There is no evidence that human and rat leprosy are identical or that human beings need fear infection from leper rats. A single experiment of mine may be detailed here, though to my mind it proves nothing one way or the other:

Centrifuged and washed suspensions of rat lepra bacilli (leper rat No. 8) were mixed with twenty-four hours' old serum from three cases of human leprosy (one very advanced nodular case, one well-developed macular case, and one of anæsthetic type) in dilutions of one-fifth, one-tenth, one-twentieth, one-fortieth, and one-eightieth with controls of normal human serum. There was no agglutination in any case in one hour at room temperature and only in one case (at one-fifth) when examined after twenty-four hours.

SUMMARY.

Most of the evidence bearing on the possible rôle of insects in the transmission of leprosy may be classified as purely a priori or as evidence based simply upon the finding of lepra-like bacilli in certain insects. It is evident that the simple taking up of parasites by an insect does not necessarily imply that the insect plays a rôle in their transmission from one host to another. Actual experiments only can demonstrate this. The leprosy disease of rats furnishes material for work of a comparative nature, and these experiments deal wholly with the fate of rat and human lepra bacilli when ingested by flies or by the larvæ of flies.

1. Flies (*C. vomitoria*, *L. Cæsar*, *M. domestica*) take up enormous numbers of lepra bacilli from the carcass of a leper rat and deposit them with their feces; but the bacilli apparently do not multiply in the flies, as the latter are clear of bacilli in less than forty-eight hours.

2. The larvæ of *C. vomitoria* hatched out in the carcass of a leper rat become heavily infested with lepra bacilli.

- (a) If such larvæ are removed and fed on uninfected meat they soon pass out most of the lepra bacilli. Such larvæ pupate and the flies hatching therefrom are generally uninfected. Occasionally a fly may deposit a few lepra bacilli after emerging from its pupa case, but it is apparently not infested in the real sense of the term.

(b) If the larvæ of *C. vomitoria* be fed almost continuously on the carcass of a leper rat they remain heavily infested with lepra bacilli. When they pupate the heavily infested pupæ seem to be incapable of undergoing further development.

3. A fly (*M. domestica*) caught on the face of a human leper was found to be infested with lepra-like bacilli. These were few in number at the beginning of the observation, but on the third day more than 1,115 lepra-like bacilli were present in each speck deposited. However, only one bacillus was found in the specks deposited between the third and sixth days. The acid-proof bacilli in this fly were not infective when injected into the subcutaneous tissue of a guinea pig.

4. The agglutinating action of blood serum from 3 human lepers was tested on washed suspensions of rat lepra bacilli with practically negative results.

Reports from San Francisco, Cal.—Plague-prevention work at San Francisco and Point Richmond.

Passed Assistant Surgeon Blue reports:

SAN FRANCISCO, CAL.

Week ended October 3.

Date of last case of plague: Sickened, January 30, 1908.

Sick inspected.....	4
Dead inspected.....	130
Premises inspected.....	15, 527
Houses disinfected.....	89
Houses destroyed.....	6
Buildings condemned.....	10
Nuisances abated.....	1, 848
<hr/>	
Rats found dead.....	482
Rats trapped.....	4, 399
<hr/>	
Total rats taken.....	4, 881
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Rats identified:	
<i>Mus norvegicus</i>	3, 558
<i>Mus rattus</i>	83
<i>Mus musculus</i>	1, 116
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Total.....	4, 757
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Rats examined bacteriologically.....	2, 883
Necropsy held.....	1
Poisons placed.....	134, 242

POINT RICHMOND, CAL.

Week ended September 26.

Premises inspected.....	492
Nuisances abated.....	10
Rats found dead.....	32
Rats trapped.....	69
Poisons placed.....	23, 800